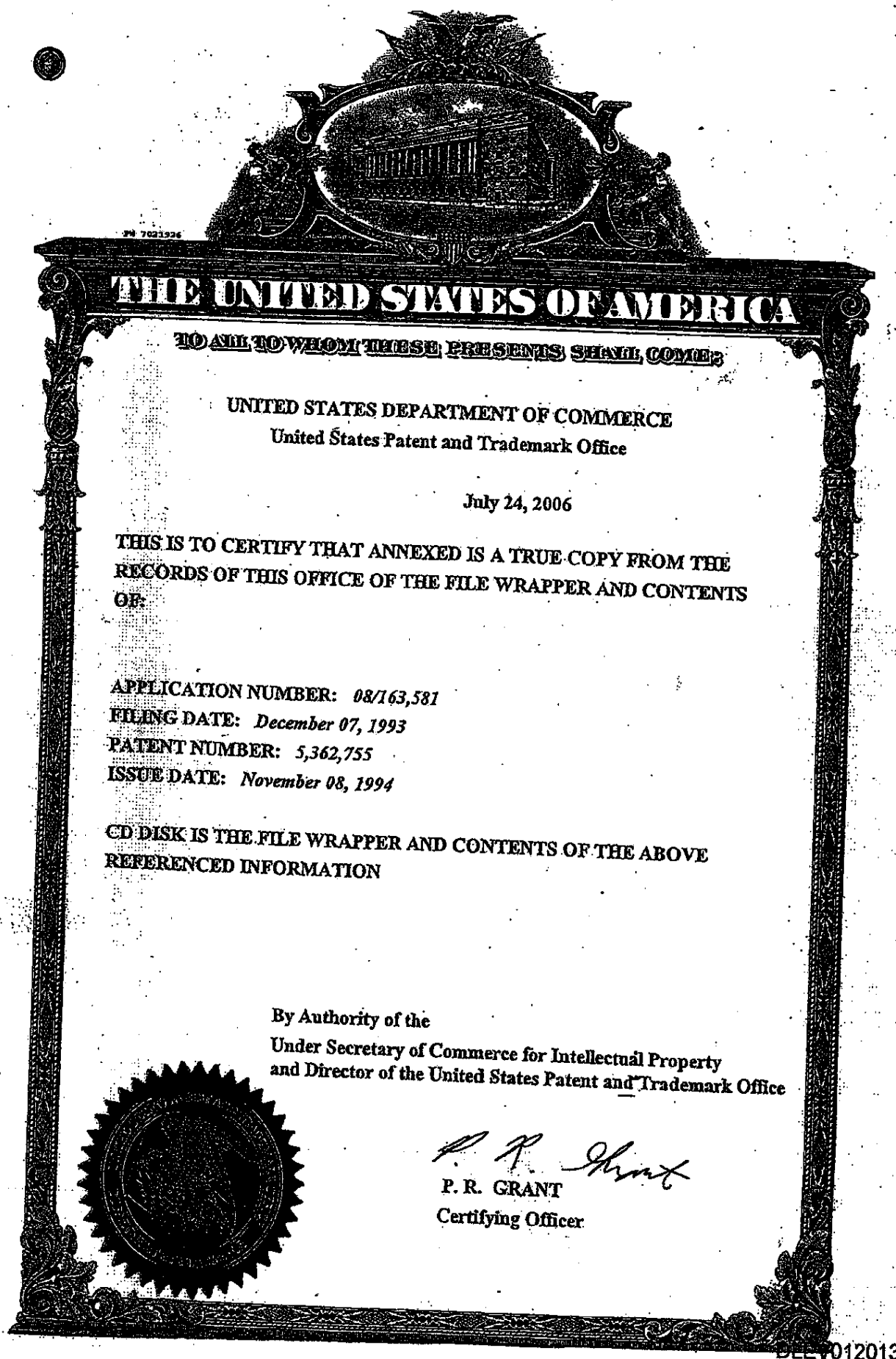


# **EXHIBIT 10**



DEE7012013

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SERIAL NUMBER 07/461,262		PATENT DATE 01/05/96		PATENT NUMBER 6005	
CLASS 514	SUBCLASS 6005	GROUP ART UNIT 125	EXAMINER Schulman		
APPLICANTS TIMOTHY J. BARBERICH, CONCORD, MA; JAMES W. YOUNG, STILL RIVER, MA.					
**CONTINUING DATA** VERIFIED					
**FOREIGN/RCT APPLICATIONS** VERIFIED					
FOREIGN FILING LICENSE GRANTED 03/29/90 ***** SMALL ENTITY *****					
Foreign priority claimed 35 USC 119 conditions met Yes <input type="checkbox"/> No <input type="checkbox"/>	AS FILED MA	STATE OR COUNTRY MA	SHEETS DRAWN 0	TOTAL CLAIMS 12	INDEP CLAIMS 3
Filing Fee Received \$ 430.00	ATTORNEY'S DOCKET NO. SPC8905				
ADDRESS HAMILTON, BROOK, SMITH & REYNOLDS TWO BELTIA DRIVE LEXINGTON, MA 02173-4799					
TITLE METHOD FOR TREATING ASTHMA USING OPTICALLY PURE R(-)-ALBUTEROL					
U.S. DEPT. OF COMM. Pat. & TM Office - PTO-4361 (rev. 10-78)					
PARTS OF APPLICATION FILED SEPARATELY					
NOTICE OF ALLOWANCE MAILED		PREPARED FOR ISSUE		CLAIMS ALLOWED	
		Assistant Examiner Docket Clerk		Total Claims Print Claim	
ISSUE FEE Amount Due Date Paid		Primary Examiner		DRAWING Sheets Drwg. Figs. Drwg. Print Fig.	
		ISSUE CLASSIFICATION Class Subclass		ISSUE BATCH NUMBER	
Label Area		WARNING: The information disclosed herein may be restricted. Unauthorized disclosure may be prohibited by the United States Code Title 35, Sections 122, 181 and 368. Possession outside the U.S. Patent & Trademark Office is restricted to authorized employees and contractors only.			

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DLEV012014

SEARCHED

## SEARCH NOTES

**INTERFERENCE SEARCHED**

DLEV012015

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## INDEX OF CLAIMS

Claim	Date
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SYMBOLS

..... Subject  
 ..... Answer  
 ..... (Through answer) Crossed  
 ..... Withdrawn  
 ..... Non-suited  
 ..... Dismissed  
 ..... Appeal  
 ..... Deposed

Claim	Date
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DLEV012016

PATENT APPLICATION  
Docket No.: SPC89-05

HAMILTON, BROOK, SMITH &amp; REYNOLDS, P.C.

TWO MILITIA DRIVE

LEXINGTON, MASSACHUSETTS 02173-4799

(617) 861-6240

461262

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MARY LOU WAKIMURA  
THOMAS O. HOOVER  
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ALICE G. OLEK  
KEVIN J. CANNING\*\*

January 5, 1990

MUNROE H. HAMILTON  
(1906-1984)

OF COUNSEL

RICHARD A. WISE

OFFICE ADMINISTRATOR

BARBARA J. FORGUE

PATENTS, TRADEMARKS

AND COPYRIGHTS

TELEX 281794

CABLE "PATENTS LXON"

FACSIMILE: (617) 861-9540

\*D.C. BAR ONLY  
\*\*GEORGIA BAR ONLY

The Honorable Commissioner  
of Patents and Trademarks  
Washington, D. C. 20231

Sir:

Transmitted herewith for filing is the patent application of

Inventor(s): Timothy J. Barberich and James W. YoungFor: METHOD FOR TREATING ASTHMA USING OPTICALLY PURE  
R(-) ALBUTEROL

- ☒ Specification, Claims, Abstract of the Disclosure
- ☐ 0 sheets of formal/informal drawings.
- ☐ An assignment of the invention to \_\_\_\_\_
- ☐ A verified statement to establish small entity status under 37 C.F.R. 1.9 and 37 C.F.R. 1.27.
- ☒ Executed/Unexecuted Combined Declaration/Power of Attorney.
- ☐ Other: \_\_\_\_\_

The filing fee has been calculated as shown below:

(Col. 1)			(Col. 2)		SMALL ENTITY		OTHER THAN A SMALL ENTITY	
FOR	NO. FILED	NO. EXTRA	RATE	FEE	RATE	FEE	RATE	FEE
BASIC FEE				\$ 185		\$ 370		
TOTAL CLAIMS	12 - 20 =	0	x 6 =	\$	x 12 =	\$ 0		
INDEP CLAIMS	3 - 3 =	0	x 18 =	\$	x 36 =	\$ 0		
<input type="checkbox"/> MULTIPLE DEPENDENT CLAIM PRESENTED			+60 =	\$	+120 =	\$		
*If the difference in Col. 1 is less than zero, enter "0" in Col. 2			Assignment Fee	\$	Assignment Fee	\$		
			TOTAL:	\$	TOTAL:	\$ 370		

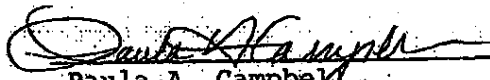
DLEV012017

Commissioner of Patents  
and Trademarks  
Page 2.

- ☐ Please charge my Deposit Account No. 08-0380 in the amount of \$\_\_\_\_\_. A duplicate copy is enclosed.
- ☒ A check in the amount of \$ 370.00 to cover the filing fee is enclosed.
- ☒ The Commissioner is hereby authorized to charge payment of the following fees associated with this communication or credit any overpayment to Deposit Account No. 08-0380. Two copies of this sheet are enclosed.
- ☒ Any additional filing fees required under 37 C.F.R. 1.16.
- ☒ Any patent application processing fees under 37 C.F.R. 1.17.
- ☒ The Commissioner is hereby authorized to charge payment of the following fees during pendency of this application or credit any overpayment to Deposit Account No. 08-0380. Two copies of this sheet are enclosed.
- ☒ Any patent application processing fees under 37 C.F.R. 1.17.
- ☒ Any filing fees under 37 C.F.R. 1.16 for presentation of extra claims.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

  
Paula A. Campbell  
Registration No. 32,503  
Attorney for Applicant(s)

Dated: January 5, 1990

DLEV012018

SPC89-05  
1/4/90PATENT APPLICATION  
DOCKET NO: SPC89-05370.00-10/14  
08/16358/METHOD FOR TREATING ASTHMA USING  
OPTICALLY PURE R(-) ALBUTEROLDescriptionBackground

05 Albuterol is a drug belonging to the general class of beta-adrenergic compounds. The prime action of beta-adrenergic drugs is to stimulate adenylyl cyclase, the enzyme which catalyzes the formation of cyclic-3',5'-adenosine monophosphate

10 (AMP) from adenosine triphosphate (ATP). The cyclic AMP formed mediates the cellular responses. Albuterol acts selectively on beta<sub>2</sub>-adrenergic receptors to relax smooth muscle tissue, for example, in the bronchial system. Albuterol is most

15 commonly used to treat bronchial spasms associated with asthma and is the active component in well-known commercial bronchodilators such as Proventil and Ventolin.

20 The form in which albuterol is presently used is a racemic mixture. That is, it is a mixture of optical isomers, called enantiomers. Enantiomers are structurally identical compounds which differ only in that one isomer is a mirror image of the other and the mirror images cannot be superimposed.

25 This phenomenon is known as chirality. Most biological molecules exist as enantiomers and exhibit chirality. Although structurally identical, enantiomers can have profoundly different effects in biological systems: one enantiomer may have a

08/16-7-90

-2-

specific biological activity while the other enantiomer has no biological activity at all, or may have an entirely different form of biological activity.

05 Summary of the Invention

31 The present invention relates to a method of treating bronchial disorders, such as asthma, in an individual, by administering to the individual an amount of optically pure R(-) albuterol which is 10 active in bronchial tissue sufficient to reduce bronchial spasms associated with asthma while minimizing side effects associated with albuterol. The method is particularly useful in treating asthma while reducing side effects, such as central nervous 15 system stimulatory effects and cardiac arrhythmia. In these applications, it is important to have a composition which is a potent broncho-dilator and which does not exhibit the adverse side effects of many beta-adrenergic drugs. A composition 31 20 containing the pure R(-) isomer of albuterol is particularly useful for this application because this isomer exhibits these desired characteristics. The present method provides a safe, effective method for treating asthma while reducing undesirable side 25 effects, for example, tremor, nervousness, shakiness, dizziness and increased appetite, and particularly, cardiac arrhythmia, typically associated with beta-adrenergic drugs. In children, side effects such as excitement, nervousness and 30 hyperkinesia are reduced when the pure isomer is

DLEV012020

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administered. In addition to the above, at certain levels racemic albuterol can cause teratogenic effects, which are believed to be associated with the S(+) isomer. Administering the pure isomer reduces the teratogenic potential which is associated with the S(+) isomer of albuterol.

#### Detailed Description of the Invention

The present invention relies on the broncho-dilation activity of the R(-) enantiomer of albuterol to provide relief from bronchial disorders, while simultaneously reducing undesirable side effects, for example, central nervous system stimulatory effects and cardiac disorders, commonly experienced by albuterol users. In the present method, the optically pure R(-) isomer of albuterol, which is substantially free of the S(+) enantiomer, is administered alone, or in combination with one or more other drug(s) in adjunctive treatment, to an individual in whom asthma relief (e.g., relief from bronchial spasms, shortness of breath) is desired. The optically pure R(-) isomer of albuterol as used herein refers to the levorotatory optically pure isomer of  $\alpha^1$ [(tert-butylamino) methyl]-4-hydroxy-m-xylene- $\alpha$ ,  $\alpha$ -diol, and to any biologically acceptable salt or ester thereof. The terms "optically pure" or "substantially free of the S(+) enantiomer" as used herein means that the composition contains at least 90% by weight of the R(-) isomer of albuterol and 10% by weight or less of the S(+) isomer. Optically pure albuterol is readily

DLEV012021

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obtainable by methods known to those of skill in the art, for example, by synthesis from an optically pure intermediate.

In the present method, the R(-) isomer of albuterol is administered to an individual who has asthma. For example, R(-) albuterol is administered to an individual after onset of asthma to reduce breathing difficulty resulting from asthma. In another embodiment, optically pure R(-) albuterol is administered prophylactically, that is, before the bronchospasm begins in an asthma attack, to prevent its occurrence or to reduce the extent to which it occurs.

In the present method, R(-) albuterol can be administered by inhalation, by subcutaneous or other injection, orally, intravenously, topically, parenterally, transdermally, rectally or via an implanted reservoir containing the drug. The form in which the drug will be administered (e.g., inhalant, powder, tablet, capsule, solution, emulsion) will depend on the route by which it is administered. The quantity of the drug to be administered will be determined on an individual basis, and will be based at least in part on consideration of the individual's size, the severity of the symptoms to be treated and the result sought. In general, quantities of optically pure R(-) albuterol sufficient to reduce the symptoms of asthma will be administered. The actual dosage (quantity administered at a time) and the number of administrations per day will depend on the mode of

DLEV012022

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31 administration, for example, by inhaler, nebulizer  
or oral administration. About 30 mcg to about 90  
mcg of the optically pure R(-) isomer of albuterol  
given by inhalation one or more times per day will  
05 be adequate in most individuals to produce the  
desired bronchodilation effect. For oral  
administration, e.g., tablet or syrup, a dose of  
about 1 mg to about 8 mg two to four times daily is  
administered to produce the desired effect.

31 10 In the method of the present invention, the  
optically pure R(-) isomer of albuterol can be  
administered together with one or more other  
drug(s). For example, an antiasthmatic drug such as  
theophylline or terbutaline, or an antihistamine or  
15 analgesic such as aspirin, acetaminophen or  
ibuprofen, can be given with or in close temporal  
proximity to administration of optically pure, R(-)  
albuterol. The two (or more) drugs (the optically  
pure active isomer of albuterol and another drug)  
20 can be administered in one composition or as two  
separate entities. For example, they can be  
administered in a single capsule, tablet, powder, or  
liquid, etc. or as individual compounds. The  
components included in a particular composition, in  
25 addition to optically pure albuterol and another  
drug or drugs, are determined primarily by the  
manner in which the composition is to be adminis-  
tered. For example, a composition to be  
administered in inhalent form can include, in  
30 addition to the drug(s), a liquid carrier and/or  
propellant. A composition to be administered in

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tablet form can include a filler (e.g., lactose), a binder (e.g., carboxymethyl cellulose, gum arabic, gelatin), an adjuvant, a flavoring agent, a coloring agent and a coating material (e.g., wax or a plasticizer). A composition to be administered in liquid form can include the combination of drugs and, optionally, an emulsifying agent, a flavoring agent and/or a coloring agent.

In general, according to the method of the present invention, the optically pure R(-) isomer of albuterol, alone or in combination with another drug(s), is administered to an individual periodically as necessary to reduce symptoms of asthma.

The present composition and method provide an effective treatment for asthma while minimizing the undesirable side effects associated with albuterol use. These side effects include central nervous system effects, such as tremor, nervousness, shakiness, dizziness and increased appetite, and cardiac effects, such as cardiac arrhythmia. In children, side effects, such as excitement, nervousness and hyperkinesia, are reduced when the pure isomer is administered. In addition, teratogenic effects associated with albuterol are believed to reside in the S(+) enantiomer. Thus, administering the pure R(-) isomer may reduce the teratogenic potential associated with albuterol.

#### Equivalents

Those skilled in the art will recognize, or be able to ascertain, using no more than routine

DLEV012024

- 7 -

experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed in the scope of the following claims.

8

Clk

declaim:

DLEV012025

-8-

CLAIMS

Sub  
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05

Ind

↑

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1. A method of treating asthma in an individual with albuterol, while reducing side effects associated with albuterol, comprising administering to the individual a quantity of an optically pure R(-) isomer of albuterol sufficient to result in bronchodilation, said R isomer being substantially free of its S(+) isomer.
- 10 2. A method of Claim 1 wherein the amount of the R(-) isomer of albuterol is greater than approximately 90% by weight *of total albuterol*.
3. A method of Claim 2 wherein the amount of the R(-) isomer of albuterol is greater than 99% by weight *of total albuterol*.
- 15 4. A method of Claim 1 comprising administering to the individual by inhalation from approximately 30 mcg to approximately 90 mcg of the R(-) isomer of albuterol per dose.
- 20 5. A method of Claim 1 comprising orally administering to the individual from approximately 1 mg to approximately 8 mg of the R(-) isomer of albuterol two to four times daily.
- 25

DLEV012026

-9-

- NK*  
*NO*
- Sub B'*
6. A method of treating asthma in an individual with albuterol, while reducing side effects associated with albuterol, comprising administering to the individual a quantity of an optically pure R(-) isomer of albuterol sufficient to result in bronchodilation and at least one additional drug.
7. A method of Claim 6 wherein the additional drug is selected from the group consisting of: bronchodilators, antihistamines and analgesics.
7. A method of Claim <sup>6</sup> wherein the analgesic is selected from the group consisting of: aspirin, acetaminophen and ibuprofen.
- B*

*End*

- Sub A'*
9. A composition comprising an optically pure R(-) isomer of albuterol and at least one additional drug.
10. A composition of Claim 9 containing at least 90% by weight of the R(-) isomer of albuterol.
11. A composition of Claim 10 containing at least 99% by weight of the R(-) isomer of albuterol.
12. A composition of Claim 9 wherein the additional drug is selected from the group consisting of: bronchodilators, antihistamines and analgesics.

*Add B<sup>3</sup>*

*Add E<sup>1</sup>*

13

08/163581

-10-

METHOD FOR TREATING ASTHMA USING  
OPTICALLY PURE R(-) ALBUTEROL

Abstract of the Disclosure

SA 31  
I  
05 The optically pure R(-) isomer of albuterol,  
which is substantially free of the S(+) isomer, is a  
potent bronchodilator for relieving the symptoms  
associated with asthma in individuals. A method is  
disclosed utilizing the optically pure R(-) isomer  
of albuterol for treating asthma while minimizing  
10 the side effects associated with <sup>chronic administration of racemic</sup> albuterol. E

DLEV012028

SPC89-05

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Declaration for Patent Application

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name;

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

METHOD FOR TREATING ASTHMA USING OPTICALLY PURE R(-)

ALBUTEROL

the specification of which (check one)

☒ is attached hereto.

☐ was filed on \_\_\_\_\_ as  
Application Serial No. \_\_\_\_\_ (if applicable)  
and was amended on \_\_\_\_\_

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s)

			Priority Claimed	
(Number)	(Country)	(Day/Month/Year filed)	<input type="checkbox"/> Yes	<input type="checkbox"/> No
(Number)	(Country)	(Day/Month/Year filed)	<input type="checkbox"/> Yes	<input type="checkbox"/> No
(Number)	(Country)	(Day/Month/Year filed)	<input type="checkbox"/> Yes	<input type="checkbox"/> No

DLEV012029

-2-

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

(Application Serial No.)	(Filing date)	(Status, patented, pending, abandoned)
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(Application Serial No.)	(Filing date)	(Status, patented, pending, abandoned)
--------------------------	---------------	--

As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith.

I also hereby grant additional Powers of Attorney to the following attorney(s) and/or agent(s) to file and prosecute an international application under the Patent Cooperation Treaty based upon the above-identified application, including a power to meet all designated office requirements for designated states.

David E. Brook	Registration No. 22,592
James M. Smith	Registration No. 28,043
Leo R. Reynolds	Registration No. 20,884
Giulio A. DeConti, Jr.	Registration No. 31,503
Richard A. Wise	Registration No. 18,041
Patricia Granahan	Registration No. 32,227
Mary Lou Wakimura	Registration No. 31,804
Thomas O. Hoover	Registration No. 32,470
Paula A. Campbell	Registration No. 32,503
Alice C. Olek	Registration No. 33,542

all of Hamilton, Brook, Smith and Reynolds, P.C., Two Militia Drive, Lexington, Massachusetts 02173;

and

6:1  
Send correspondence to: Patricia Granahan, Esq.  
HAMILTON, BROOK, SMITH & REYNOLDS, P.C.  
Two Militia Drive, Lexington, Massachusetts 02173

762  
Direct telephone calls to: Patricia Granahan, Esq.

617-861-6240

DLEV012030

-3-

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of sole  
or first inventor Timothy J. Barberich  
Inventor's  
Signature [Signature] Date \_\_\_\_\_  
Residence 73 Nashoba Road  
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Citizenship USA  
Post Office Address SAME

Full name of second joint  
inventor, if any James W. Young  
Second Inventor's  
Signature \_\_\_\_\_ Date \_\_\_\_\_  
Residence 295 Still River Road  
Still River, Massachusetts 01467  
Citizenship USA  
Post Office Address SAME

Full name of third joint  
inventor, if any \_\_\_\_\_  
Third Inventor's  
Signature \_\_\_\_\_ Date \_\_\_\_\_  
Residence \_\_\_\_\_  
Citizenship \_\_\_\_\_  
Post Office Address \_\_\_\_\_

Full name of fourth joint  
inventor, if any \_\_\_\_\_  
Fourth Inventor's  
Signature \_\_\_\_\_ Date \_\_\_\_\_  
Residence \_\_\_\_\_  
Citizenship \_\_\_\_\_  
Post Office Address \_\_\_\_\_

DLEV012031

EXHIBIT APPLICATION  
SPC89-05



UNITED STATES APPLICATION FOR LETTERS PATENT

Inventor(s): Timothy J. Barberich and James W. Young

Attorney's Docket No.: SPC89-05

Title: METHOD FOR TREATING ASTHMA USING OPTICALLY PURE  
R(-) ALBUTEROL

EXPRESS MAIL Mailing Label No. RB353218822

Date of Deposit January 5, 1990

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. 1.10 on the date indicated above and is addressed to the Commissioner of Patents and Trademarks, Washington, D. C. 20231.

Susan D. Dellarocco

(Typed or printed name of person mailing paper or fee)

Susan D. Dellarocco

(Signature of person mailing paper or fee)

DLEV012032

Form PTO-875 REV. 1-85	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	SERIAL NO. 461262	FILED DATE 1-5-90
PATENT APPLICATION FEE DETERMINATION RECORD		APPLICANT (FIRST NAME) Barberich et al	

## CLAIMS AS FILED - PART I

FOR	NO FILED	NO EXTRA
BASIC FEE		
TOTAL CLAIMS	12	
INDEP. CLAIMS	3	
MULTIPLE DEPENDENT CLAIMS PRESENT		

\* If the difference in Col. 1 is less than 20% enter "0" in Col. 2.

## SMALL ENTITY

RATE	FEE
	\$ 185
x 6	\$
x 18	\$
60	\$
TOTAL	\$

OTHER THAN A  
SMALL ENTITY

RATE	FEE
	\$ 370
x 12	\$
x 36	\$
120	\$
TOTAL	\$ 570

## CLAIMS AS AMENDED - PART II

AMENDMENT A		CLAIMS REMAINING AFTER AMENDMENT	MINUS	HIGHEST NO. PREVIOUSLY PAID FOR	PRESENT EXTRA
	TOTAL	10		20	-
	INDEP.	3		3	-
FIRST PRESENTATION OF MULTIPLE DEP. CLAIM					

## SMALL ENTITY

RATE	ADDIT. FEE
x 6	\$
x 18	\$
60	\$
TOTAL ADDIT. FEE	\$

OTHER THAN A  
SMALL ENTITY

RATE	ADDIT. FEE
x 12	\$
x 36	\$
120	\$
TOTAL	\$

AMENDMENT B		CLAIMS REMAINING AFTER AMENDMENT	MINUS	HIGHEST NO. PREVIOUSLY PAID FOR	PRESENT EXTRA
	TOTAL				
	INDEP.				
FIRST PRESENTATION OF MULTIPLE DEP. CLAIM					

RATE	ADDIT. FEE
x 6	\$
x 18	\$
60	\$
TOTAL ADDIT. FEE	\$

RATE	ADDIT. FEE
x 12	\$
x 36	\$
120	\$
TOTAL	\$

AMENDMENT C		CLAIMS REMAINING AFTER AMENDMENT	MINUS	HIGHEST NO. PREVIOUSLY PAID FOR	PRESENT EXTRA
	TOTAL				
	INDEP.				
FIRST PRESENTATION OF MULTIPLE DEP. CLAIM					

RATE	ADDIT. FEE
x 6	\$
x 18	\$
60	\$
TOTAL ADDIT. FEE	\$

RATE	ADDIT. FEE
x 12	\$
x 36	\$
120	\$
TOTAL	\$

DLEV012033


**UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office**

 Address: COMMISSIONER OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
---------------	-------------	-----------------------	------------------

07/461,262 01/05/90 BARBERICH T SPC8905

 HAMILTON, BROOK, SMITH & REYNOLDS  
TWO HILTYA DRIVE  
LEXINGTON, MA 02173-4799

01/24/90

DATE MAILED:

**NOTICE TO FILE MISSING PARTS OF APPLICATION—  
FILING DATE GRANTED**

A filing date has been granted to this application. However, the following parts are missing:

 If all missing parts are filed within the period set below, the total amount owed by applicant as a ☒ large entity, ☐ small entity (verified statement filed), is \$ 120.00

 1. ☐ The statutory basic filing fee is: ☐ missing, ☐ insufficient. Applicant as a ☐ large entity, ☐ small entity, must submit \$ \_\_\_\_\_ to complete the basic filing fee and **MUST ALSO SUBMIT THE SURCHARGE AS INDICATED BELOW.**

 2. ☐ Additional claim fees of \$ \_\_\_\_\_ as a ☐ large entity, ☐ small entity, including any required multiple dependent claim fee, are required. Applicant must submit the additional claim fees or cancel the additional claims for which fees are due. **NO SURCHARGE IS REQUIRED FOR THIS ITEM.**

 3. ☒ The oath or declaration:

☐ is missing.

☐ does not cover items omitted at the time of execution.

 An oath or declaration in compliance with 37 CFR 1.63, identifying the application by the above Serial Number and Filing Date is required. **A SURCHARGE MUST ALSO BE SUBMITTED AS INDICATED BELOW.**

 4. ☐ The oath or declaration does not identify the application to which it applies. An oath or declaration in compliance with 37 CFR 1.63 identifying the application by the above Serial Number and Filing Date is required. **A SURCHARGE MUST ALSO BE SUBMITTED AS INDICATED BELOW.**

 5. ☐ The signature to the oath or declaration is: ☐ missing, ☐ a reproduction, ☐ by a person other than the inventor or a person qualified under 37 CFR 1.42, 1.43, or 1.47. A properly signed oath or declaration in compliance with 37 CFR 1.63, identifying the application by the above Serial Number and Filing Date is required. **A SURCHARGE MUST ALSO BE SUBMITTED AS INDICATED BELOW.**

 6. ☐ The signature of the following joint inventor(s) is missing from the oath or declaration: \_\_\_\_\_ Applicant(s) should provide, if possible an oath or declaration signed by the omitted inventor(s), identifying this application by the above Serial Number and Filing Date. **A SURCHARGE MUST ALSO BE SUBMITTED AS INDICATED BELOW.**

 7. ☐ The application was filed in a language other than English. Applicant must file a verified English translation of the application and a fee of \$26.00 under 37 CFR 1.17(b), unless this fee has already been paid. **NO SURCHARGE UNDER 37 CFR 1.16(e) IS REQUIRED FOR THIS ITEM.**

 8. ☐ A \$20.00 processing fee is required for returned checks. (37 CFR 1.21(m)).

 9. ☐ Your filing receipt was mailed in error because check was returned.

 10. ☐ Other:

 A Serial Number and Filing Date have been assigned to this application. However, to avoid abandonment under 37 CFR 1.53(d), the missing parts and fees identified above in items 1 and 3-6 must be timely provided **ALONG WITH THE PAYMENT OF A SURCHARGE OF \$120.00** for large entities or \$60.00 for small entities who have filed a verified statement claiming such status. The surcharge is set forth in 37 CFR 1.16(e). Applicant is given **ONE MONTH FROM THE DATE OF THIS LETTER, OR TWO MONTHS FROM THE FILING DATE** of this application, **WHICHEVER IS LATER**, within which to file all missing parts and pay any fees. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

Direct the response to, and any questions about, this notice to the undersigned, Attention: Application Branch.

**A copy of this notice MUST be returned with response.**

 For: Manager, Application Branch  
(703) 557-2235

FORM PTO-623 (REV. 7-87)

OFFICE C

**For Office Use Only**
☐ 102 ☐ 202  
☐ 103 ☐ 203  
☐ 104 ☐ 204  
☐ 105 ☐ 205

DLEV012034

SPC89-05



## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Declaration for Patent Application

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name;

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

METHOD FOR TREATING ASTHMA USING OPTICALLY PURE R(-)

ALBUTEROL

the specification of which (check one)

☐ is attached hereto.

☒ was filed on January 5, 1990 as  
Application Serial No. 07/461,262 (if applicable).  
and was amended on \_\_\_\_\_

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s)

(Number)	(Country)	(Day/Month/Year filed)	Priority Claimed	
_____	_____	_____	<input type="checkbox"/> Yes	<input type="checkbox"/> No
_____	_____	_____	<input type="checkbox"/> Yes	<input type="checkbox"/> No
_____	_____	_____	<input type="checkbox"/> Yes	<input type="checkbox"/> No

DLEV012035

-2-

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

(Application Serial No.)	(Filing date)	(Status, patented, pending, abandoned)
(Application Serial No.)	(Filing date)	(Status, patented, pending, abandoned)

As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith.

I also hereby grant additional Powers of Attorney to the following attorney(s) and/or agent(s) to file and prosecute an international application under the Patent Cooperation Treaty based upon the above-identified application, including a power to meet all designated office requirements for designated states.

David E. Brook	Registration No. <u>22,592</u>
James M. Smith	Registration No. <u>28,043</u>
Leo R. Reynolds	Registration No. <u>20,884</u>
Giulio A. DeConti, Jr.	Registration No. <u>31,503</u>
Richard A. Wise	Registration No. <u>18,041</u>
Patricia Granahan	Registration No. <u>32,227</u>
Mary Lou Wakimura	Registration No. <u>31,804</u>
Thomas O. Hoover	Registration No. <u>32,470</u>
Paula A. Campbell	Registration No. <u>32,503</u>
Alice C. Olek	Registration No. <u>33,542</u>

all of Hamilton, Brook, Smith and Reynolds, P.C., Two Militia Drive, Lexington, Massachusetts 02173;

and

605  
701  
Send correspondence to: Patricia Granahan, Esq.  
HAMILTON, BROOK, SMITH & REYNOLDS, P.C.  
Two Militia Drive, Lexington, Massachusetts 02173

701  
Direct telephone calls to: Patricia Granahan, Esq.

617-861-6240

DLEV012036

-3-

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of sole 401-PP  
 or first inventor Timothy J. Barberich  
 Inventor's  
 Signature Timothy Barberich Date 2/28/90  
 Residence 73 Nashoba Road  
Concord, Massachusetts 01742 MA  
 Citizenship USA  
 Post Office Address SAME

Full name of second joint 402-PP  
 inventor, if any James W. Young  
 Second Inventor's  
 Signature James W. Young Date 1 March 90  
 Residence 295 Still River Road  
Still River, Massachusetts 01467 MA  
 Citizenship USA  
 Post Office Address SAME

Full name of third joint  
 inventor, if any  
 Third Inventor's  
 Signature \_\_\_\_\_ Date \_\_\_\_\_  
 Residence \_\_\_\_\_  
 Citizenship \_\_\_\_\_  
 Post Office Address \_\_\_\_\_

Full name of fourth joint  
 inventor, if any  
 Fourth Inventor's  
 Signature \_\_\_\_\_ Date \_\_\_\_\_  
 Residence \_\_\_\_\_  
 Citizenship \_\_\_\_\_  
 Post Office Address \_\_\_\_\_

DLEV012037



Applicant for Patentee: Timothy J. Barberich and James W. Young Attorney's  
 Serial or Patent No.: 07/461,262 Docket No.: SPC89-05  
 Filed or Issued: January 5, 1990  
 For: METHOD FOR TREATING ASTHMA USING OPTICALLY PURE R(-) ALBUTEROL

**VERIFIED STATEMENT (DECLARATION) CLAIMING SMALL ENTITY STATUS**  
**(37 CFR 1.9(f) and 1.27(c) - SMALL BUSINESS CONCERN)**

I hereby declare that I am

- ☐ the owner of the small business concern identified below:  
☒ an official of the small business concern empowered to act on behalf  
 of the concern identified below:

NAME OF CONCERN Sepracor, Inc.  
 ADDRESS OF CONCERN 33 Locke Drive  
Marlborough, MA 01752

I hereby declare that the above identified small business concern qualifies as a small business concern as defined in 13 CFR 121.3-18, and reproduced in 37 CFR 1.9(d), for purposes of paying reduced fees under section 41(a) and (b) of Title 35, United States Code, in that the number of employees of the concern, including those of its affiliates, does not exceed 500 persons. For purposes of this statement, (1) the number of employees of the business concern is the average over the previous fiscal year of the concern of the persons employed on a full-time, part-time or temporary basis during each of the pay periods of the fiscal year, and (2) concerns are affiliates of each other when either, directly or indirectly, one concern controls or has the power to control the other, or a third party or parties controls or has the power to control both.

I hereby declare that rights under contract or law have been conveyed to and remain with the small business concern identified above with regard to the invention, entitled METHOD FOR TREATING ASTHMA USING OPTICALLY PURE R(-)

ALBUTEROL by inventor(s) Timothy J. Barberich and  
James W. Young

described in

- ☐ the specification filed herewith  
☒ application serial no. 07/461,262, filed January 5, 1990  
☐ patent no. \_\_\_\_\_, issued \_\_\_\_\_

-2-

If the rights held by the above identified small business concern are not exclusive, each individual, concern or organization having rights to the invention is listed below\* and no rights to the invention are held by a person, other than the inventor, who could not qualify as a small business concern under 37 CFR 1.9 (d) or by any concern which would not qualify as a small business concern under 37 CFR 1.9 (d) or a nonprofit organization under 37 CFR 1.9(e). \*NOTE: Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27)

NAME \_\_\_\_\_

ADDRESS \_\_\_\_\_

☐ INDIVIDUAL ☐ SMALL BUSINESS CONCERN ☐ NONPROFIT ORGANIZATION

NAME \_\_\_\_\_

ADDRESS \_\_\_\_\_

☐ INDIVIDUAL ☐ SMALL BUSINESS CONCERN ☐ NONPROFIT ORGANIZATION

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b))

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

NAME OF PERSON SIGNING Victor H. WoolleyTITLE OF PERSON OTHER THAN OWNER Vice President, FinanceADDRESS OF PERSON SIGNING 33 Locke Drive, Marlborough, MA 01752

SIGNATURE

Victor H. Woolley

DATE \_\_\_\_\_

DLEV012039

SPC89-05

COPY



Applicant or Patentee: Timothy J. Barberich and James W. Young Attorney's  
 or Patent No.: 07/461,262 Docket No.: SPC89-05  
 or Issued: January 5, 1990  
 For: METHOD FOR TREATING ASTHMA USING OPTICALLY PURE R(-) ALBUTEROL

**VERIFIED STATEMENT (DECLARATION) CLAIMING SMALL ENTITY STATUS**  
**(37 CFR 1.9(f) and 1.27(c) - SMALL BUSINESS CONCERN)**

I hereby declare that I am

- ☐ the owner of the small business concern identified below:  
☒ an official of the small business concern empowered to act on behalf  
 of the concern identified below:

NAME OF CONCERN Sepracor, Inc.  
 ADDRESS OF CONCERN 33 Locke Drive  
Marlborough, MA 01752

I hereby declare that the above identified small business concern qualifies as a small business concern as defined in 13 CFR 121.3-18, and reproduced in 37 CFR 1.9(d), for purposes of paying reduced fees under section 41(a) and (b) of Title 35, United States Code, in that the number of employees of the concern, including those of its affiliates, does not exceed 500 persons. For purposes of this statement, (1) the number of employees of the business concern is the average over the previous fiscal year of the concern of the persons employed on a full-time, part-time or temporary basis during each of the pay periods of the fiscal year, and (2) concerns are affiliates of each other when either, directly or indirectly, one concern controls or has the power to control the other, or a third party or parties controls or has the power to control both.

I hereby declare that rights under contract or law have been conveyed to and remain with the small business concern identified above with regard to the invention, entitled METHOD FOR TREATING ASTHMA USING OPTICALLY PURE R(-) ALBUTEROL by inventor(s) Timothy J. Barberich and

James W. Young

described in

- ☐ the specification filed herewith  
☒ application serial no. 07/461,262, filed January 5, 1990  
☐ patent no. \_\_\_\_\_, issued \_\_\_\_\_

DLEV012040

-2-

If the rights held by the above identified small business concern are not exclusive, each individual, concern or organization having rights to the invention is listed below\* and no rights to the invention are held by any person, other than the inventor, who could not qualify as a small business concern under 37 CFR 1.9 (d) or by any concern which would not qualify as a small business concern under 37 CFR 1.9 (d) or a nonprofit organization under 37 CFR 1.9(e). \*NOTE: Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27)

NAME \_\_\_\_\_

ADDRESS \_\_\_\_\_

☐ INDIVIDUAL ☐ SMALL BUSINESS CONCERN ☐ NONPROFIT ORGANIZATION

NAME \_\_\_\_\_

ADDRESS \_\_\_\_\_

☐ INDIVIDUAL ☐ SMALL BUSINESS CONCERN ☐ NONPROFIT ORGANIZATION

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b))

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

NAME OF PERSON SIGNING Victor H. WoolleyTITLE OF PERSON OTHER THAN OWNER Vice President, FinanceADDRESS OF PERSON SIGNING 33 Locke Drive, Marlborough, MA 01752SIGNATURE Victor H. Woolley

DATE \_\_\_\_\_

DLEV012041

DOCKET NO. SPC89-05 30.00-215 PATENT APPLICATION  
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE *A/N*

Applicant(s): Timothy J. Barberich and James W. Young

Serial 07/461,262

Group Art Unit:

Filed 28 MAR 9 January 5, 1990

Examiner:

For: METHOD FOR TREATING ASTHMA USING OPTICALLY  
ALBUTEROL

**RECEIVED**

MAR 22 1990

APPLICATION BRANCH

PETITION FOR EXTENSION OF TIME

The Honorable Commissioner  
of Patents and Trademarks  
Washington, D. C. 20231

Sir:

The undersigned attorney petitions the Commissioner of Patents and Trademarks to extend the time for filing a Response to the Notice to File Missing Parts dated January 24, 1990 for 1 months from March 5, 1990 to April 5, 1990.

	<u>Small Entity</u>	<u>Other than Small Entity</u>
1 month -	<u>X</u> \$ 31	\$ 62
2 months -	\$ 90	\$180
3 months -	\$215	\$430
4 months -	\$340	\$680

☒ Enclosed is a check in the amount of \$ 31.00 to cover the cost of the extension.

☐ Please charge Deposit Account No. 08-0380 in the amount of \$        to cover the cost of the extension fee.

Any deficiency or overpayment should be charged or credited to Deposit Account No. 08-0380. A duplicate copy of this letter is enclosed.

Respectfully submitted,

*Paula A. Campbell*  
Paula A. Campbell

Attorney for Applicant(s)

Registration No. 32,503

Telephone: (617) 861-6240

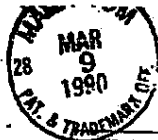
Dated: March 6, 1990  
Lexington, Massachusetts 02173

050 03/19/90 07461262

1 215

31.00 CK

DLEV012042



UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office

Address: COMMISSIONER OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
07/461,762	01/05/90	BARBERICH	T SPC8905

HAMILTON, BROOK, SMITH & REYNOLDS  
240 HILTYA DRIVE  
LEXINGTON, MA 02173-4799

000  
01/24/90

DATE MAILED:

**NOTICE TO FILE MISSING PARTS OF APPLICATION—  
FILING DATE GRANTED**

A filing date has been granted to this application. However, the following parts are missing.

If all missing parts are filed within the period set below, the total amount owed by applicant as a ☒ small entity (verified statement filed), is \$ 120.00

1. ☐ The statutory basic filing fee is: ☐ missing ☐ insufficient. Applicant as a ☐ large entity, ☐ small entity, must submit \$ \_\_\_\_\_ to complete the basic filing fee and MUST ALSO SUBMIT THE SURCHARGE AS INDICATED BELOW.
2. ☐ Additional claim fees of \$ \_\_\_\_\_ as a ☐ large entity, ☐ small entity, including any required multiple dependent claim fees, are required. Applicant must submit the additional claim fees or cancel the additional claims for which fees are due. NO SURCHARGE IS REQUIRED FOR THIS ITEM.
3. ☒ The oath or declaration: ☒ is missing.  
☐ does not cover items omitted at the time of execution.  
An oath or declaration in compliance with 37 CFR 1.63, identifying the application by the above Serial Number and Filing Date is required. A SURCHARGE MUST ALSO BE SUBMITTED AS INDICATED BELOW.
4. ☐ The oath or declaration does not identify the application to which it applies. An oath or declaration in compliance with 37 CFR 1.63 identifying the application by the above Serial Number and Filing Date is required. A SURCHARGE MUST ALSO BE SUBMITTED AS INDICATED BELOW.
5. ☐ The signature to the oath or declaration is: ☐ missing; ☐ a reproduction; ☐ by a person other than the inventor or a person qualified under 37 CFR 1.42, 1.43, or 1.47. A properly signed oath or declaration in compliance with 37 CFR 1.63, identifying the application by the above Serial Number and Filing Date is required. A SURCHARGE MUST ALSO BE SUBMITTED AS INDICATED BELOW.
6. ☐ The signature of the following joint inventor(s) is missing from the oath or declaration: \_\_\_\_\_ Applicant(s) should provide, if possible an oath or declaration signed by the omitted inventor(s), identifying this application by the above Serial Number and Filing Date. A SURCHARGE MUST ALSO BE SUBMITTED AS INDICATED BELOW.
7. ☐ The application was filed in a language other than English. Applicant must file a verified English translation of the application and a fee of \$26.00 under 37 CFR 1.17(k), unless this fee has already been paid. NO SURCHARGE UNDER 37 CFR 1.16(e) IS REQUIRED FOR THIS ITEM.
8. ☐ A \$20.00 processing fee is required for returned checks. (37 CFR 1.21(m)).
9. ☐ Your filing receipt was mailed in error because check was returned.
10. ☐ Other:

A Serial Number and Filing Date have been assigned to this application. However, to avoid abandonment under 37 CFR 1.53(d), the missing parts and fees identified above in items 1 and 3-6 must be timely provided ALONG WITH THE PAYMENT OF A SURCHARGE OF \$140.00 for large entities or \$60.00 for small entities who have filed a verified statement claiming such status. The surcharge is set forth in 37 CFR 1.15(e). Applicant is given ONE MONTH FROM THE DATE OF THIS LETTER, OR TWO MONTHS FROM THE FILING DATE of this application, WHICHEVER IS LATER, within which to file all missing parts and pay any fees. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

Direct the response to, and any questions about, this notice to the undersigned, Attention: Application Branch.

**A copy of this notice MUST be returned with response.**

For: Manager, Application B-  
(703) 557-3254

FORM PTO-1450 (REV. 1-89)

For Office Use Only  
☐ 101 ☐ 202

DLEV012043

PC89-05

PATENT APPLICATION

A/N



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Timothy J. Barberich and James W. Young

Serial No.: 07/461,262

Filed: January 5, 1990

For: METHOD FOR TREATING ASTHMA USING OPTICALLY PURE R-ALBUTEROL

TRANSMITTAL OF VERIFIED STATEMENT

The Honorable Commissioner  
of Patents and Trademarks  
Washington, D. C. 20231

Sir:

Please file the enclosed Verified Statement Claiming Small Entity Status in the above-identified patent application.

Two duplicate copies are enclosed for accounting purposes.

Respectfully submitted,

Paula A. Campbell

Registration No. 32,503

Attorney for Applicants

Lexington, MA 02173

Dated: March 6, 1990

050 03/19/90 07461262

1 205

60.00 CK

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being  
dispatched with the United States Postal Service as First  
Class Mail in an envelope addressed to Honorable  
Commissioner of Patents and Trademarks, Washington,  
D.C. 20231, on 3-6-90

Hamilton, Brook, Smith & Reynolds

*Signature*  
Date 3-6-90

DLEV012044

SPC89-05  
PAC/sld  
PAC19  
3/6/90



PATENT APPLICATION

#3

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Timothy J. Barberich and James W. Young

Serial No.: 07/461,262

Filed: January 5, 1990

For: METHOD FOR TREATING ASTHMA USING OPTICALLY  
PURE R(-) ALBUTEROL

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being  
deposited with the United States Postal Service as First  
Class Mail in an envelope addressed to Honorable  
Commissioner of Patents and Trademarks, Washington,  
D.C. 20231, on 3-6-90.  
Hamilton, Brook, Smith & Reynolds

Susan DeLaune  
Signature

3-6-90  
Date

TRANSMITTAL OF DECLARATION/POWER OF ATTORNEY

The Honorable Commissioner  
of Patents and Trademarks  
Washington, DC 20231

Sir:

Transmitted herewith is an executed  
Declaration/Power of Attorney document for filing in the

DLEV012045


-2-

above-referenced case. A copy of the Notice to File Missing Parts of Application, mailed from the Patent Office January 24, 1990, is enclosed. A check in the amount of \$60 is enclosed for the surcharge for filing the Declaration/Power of Attorney later than the filing date of the application.

Also enclosed is a copy of the Verified Statement Claiming Small Entity Status (37 C.F.R. 1.9(f) and 1.27(c) - Small Business Concern, which is being filed concurrently.

Please charge any additional fees due in this matter to Applicants' Attorney's Deposit Account No. 08-0380.

Respectfully submitted,

  
Paula A. Campbell  
Registration No. 32,503  
Attorney for Applicants  
617-861-6240

Dated: March 6, 1990  
Lexington, MA 02173

DLEV012046

SPC89-05 Req.  
PAC/sdd  
PAC19  
4/6/90



PATENT APPLICATION

RECEIVED

90 MAY -2 AM 9:21

GROUP 120

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Timothy J. Barberich and James W. Young

Serial No.: 07/461,262

Group Art Unit: 125

Filed: January 5, 1990

For: METHOD FOR TREATING ASTHMA USING OPTICALLY  
PURE R(-) ALBUTEROL

**CERTIFICATE OF MAILING**

I hereby certify that this correspondence is being  
deposited with the United States Postal Service as First  
Class Mail in an envelope addressed to Honorable  
Commissioner of Patents and Trademarks, Washington,  
D.C. 20231, on 4-11-90.

Hamilton, Brook, Smith & Reynolds

Susan Demaree  
Signature

4-11-90  
Date

**REQUEST FOR CORRECTED OFFICIAL FILING RECEIPT**

The Honorable Commissioner  
of Patents and Trademarks  
Washington, DC 20231

Sir:

RECEIVED

APR 23 1990

APPLICATION DIVISION-402

The Official Filing Receipt for the above-captioned  
patent application (a copy of which is attached) contains

DLEV012047

*per mail  
5-22-90  
LJ*

-2-

an erroneous filing date. The filing date reflected on the attached filing receipt is January 5, 1989. The correct filing date is January 5, 1990. Please send us a corrected official filing receipt.

Respectfully submitted,



Paula A. Campbell

Registration No. 32,503

Attorney for Applicants

617-861-6240

Dated: April 11, 1990  
Lexington, MA 02173

DLEV012048

PTO-103X  
(Rev. 11-88)

FILING RECEIPT

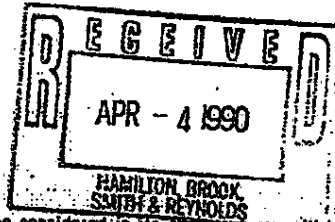
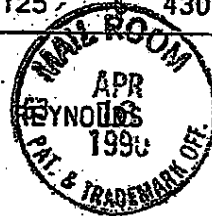


UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office  
ASSISTANT SECRETARY AND COMMISSIONER  
OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

RECEIVED

SERIAL NUMBER	FILING DATE	GRP ART UNIT	FIL FEE REC'D	ATTORNEY DOCKET NO.	RECEIVED
07/461,262	01/05/89	125	430.00	SPC8905	GROUP 120 3

HAMILTON, BROOK, SMITH &  
TWO MILITIA DRIVE  
LEXINGTON, MA 02173-4799



Receipt is acknowledged of the patent application identified herein. It will be considered in its order and you will be notified as to the examination thereof. Be sure to give the U.S. SERIAL NUMBER, DATE OF FILING, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this transmittal.

Applicant(s)

TIMOTHY J. BARBERICH, CONCORD, MA; JAMES W. YOUNG,  
STILL RIVER, MA.

FOREIGN FILING LICENSE GRANTED 03/29/90

\* SMALL ENTITY \*

TITLE

METHOD FOR TREATING ASTHMA USING OPTICALLY PURE R(-) ALBUTEROL

PRELIMINARY CLASS: 514

(see reverse)

DLEV012049

LICENSE FOR FOREIGN FILING UNDER  
Title 35, United States Code, Section 184  
Title 37, Code of Federal Regulations, 5.11

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "FOREIGN FILING LICENSE GRANTED" followed by a date appears on the reverse side of this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required. The scope and limitations of this license are set forth in 36 CFR 5.15(a). This license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license has been granted under 37 CFR 5.13.

This license is to be retained by the licensee and may be used at anytime on or after the effective date thereof unless it is revoked. The license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations, especially with respect to certain countries, of other agencies, particularly the Office of Munitions Control, Department of State (with respect to Arms, Munitions and Implements War (22 CFR, Parts 121-128)); the Office of Export Administration, Department of Commerce (15 CFR 370.10(j)); and the Department of Energy or its successors.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "FOREIGN FILING LICENSE GRANTED" DOES NOT appear on the reverse side of this form. Applicant may still petition for a license under 37 CFR 5.12(b), if a license is desired.

UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark OfficeAddress: COMMISSIONER OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	INVENTOR(S)	ATTORNEY
07/461,262	01/03/90	BARBERICH	SPC8905

HAMILTON, BROOK, SMITH & REYNOLDS  
TWO MILITIA DRIVE  
LEXINGTON, MA 02173-4799

SCHENKMAN, L.

JAY QAK: PAPER BARBER

125

08/20/90

This is a common action form the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS
☒ This application has been examined. ☐ Responsive to communication filed on: ☐ This action is made final.
A shortened statutory period for response to this action is set to expire 13 month(s) from the date of this letter.  
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

## Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

- ☒ Notice of References Cited by Examiner, PTO-892.
- ☐ Notice re Patent Drawing, PTO-848.
- ☐ Notice of Art Cited by Applicant, PTO-1449.
- ☐ Notice of Informal Patent Application, Form PTO-152
- ☐ Information on How to Effect Drawing Changes, PTO-1474.
- ☐

## Part II SUMMARY OF ACTION

- ☒ Claims 1-12 are pending in the application.  
Of the above, claims \_\_\_\_\_ are withdrawn from consideration.
- ☐ Claims \_\_\_\_\_ have been cancelled.
- ☐ Claims \_\_\_\_\_ are allowed.
- ☒ Claims 1-12 are rejected.
- ☐ Claims \_\_\_\_\_ are objected to.
- ☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.
- ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
- ☐ Formal drawings are required in response to this Office action.
- ☐ The corrected or substitute drawings have been received on \_\_\_\_\_. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-848).
- ☐ The proposed additional or substitute sheet(s) of drawings, filed on \_\_\_\_\_, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
- ☐ The proposed drawing correction, filed \_\_\_\_\_, has been: ☐ approved; ☐ disapproved (see explanation).
- ☐ Acknowledgement is made of the claims for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. \_\_\_\_\_; filed on \_\_\_\_\_.
- ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
- ☐ Other

PTOL-328 (Rev. 5-89)

EXAMINER'S ACTION

DLEV012051

Serial No. 07/461,262

-2-

Art Unit 125

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-12 are rejected under 35 U.S.C. § 103 as being unpatentable over the Chemical Abstracts reference which teaches salbutamol (albuterol) used to treat asthma and compositions containing same. The determination of a particular isomer to employ would be a matter of obvious, alternatives to one skilled in the art. Allegations of reduced side effects are not persuasive since this has not been clinically established. Further, difference in activity between isomers is not unexpected; see *In re Adamson et al*, 125 USPQ 233.

Claims 9-12 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims lack proportions of

DLEV012052

Serial No. 07/461,262

-3-

Art Unit 125

ingredients. The amount of the R isomer appears to relate to the entire composition rather than total albuterol.

  
LEONARD SCHENKMAN  
EXAMINER  
ART UNIT 125

Schenkman:st  
August 10, 1990

DLEV012053

08/16/03, 581

FORM PTO-892 (REV. 3-78) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

NOTICE OF REFERENCES CITED

SERIAL NO. 07/461,122 GROUP ART UNIT 12.5 ATTACHMENT TO PAPER NUMBER 1

APPLICANT(S) BARBERICH ET AL

U.S. PATENT DOCUMENTS

	DOCUMENT NO.	DATE	NAME	CLASS	SUB-CLASS	FILING DATE IF APPROPRIATE
A						
B						
C						
D						
E						
F						
G						
H						
I						
J						
K						

FOREIGN PATENT DOCUMENTS

	DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	SUB-CLASS	PERTINENT SMTS. FIGS. SPEC.
L							
M							
N							
O							
P							
Q							

OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

R	CHEMICAL ABSTRACTS 89: 123259m (1970)
S	
T	
U	

EXAMINER J. J. J. DATE 8-18-70

\* A copy of this reference is not being furnished with this office action.  
(See Manual of Patent Examining Procedure, section 707.05 (a).)

DLEV012054

PATENT APPLICATION  
DOCKET NO.: SPC89-05

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Timothy J. Barberich and James W. Young

Serial No.: 07/461,262

Group Art Unit: 125

Filed: January 5, 1990

Examiner: L. Schenkman

For: METHOD FOR TREATING ASTHMA USING OPTICALLY PURE  
R(-) ALBUTEROL

## CERTIFICATE OF MAILING

I hereby certify that this correspondence is being  
deposited with the United States Postal Service as First  
Class Mail in an envelope addressed to Honorable  
Commissioner of Patents and Trademarks, Washington,  
D.C. 20231, on 12-20-90

The Honorable Commissioner of  
Patents and Trademarks  
Washington, D.C. 20231

Hamilton, Brook, Smith &amp; Reynolds

Susan Dellamora  
Signature

12-20-90  
Date

Sir:

Transmitted herewith is a response in the above-identified  
application.

☒ Small entity status of this application under 37 C.F.R. 1.9  
and 1.27 has been established by a verified statement  
previously submitted.

☐ A verified statement to establish small entity status under  
37 C.F.R. 1.9 and 1.27 is enclosed.

The fee has been calculated as shown below:

(Col. 1)		(Col. 2) (Col. 3)		SMALL ENTITY		OR	OTHER THAN SMALL ENTITY	
CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NO. PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE	ADDIT. FEE		RATE	ADDIT. FEE
TOTAL 12	MINUS	** 20	= 0	x 10	\$		x 20	\$
NDEP. 3	MINUS	*** 3	= 0	x 30	\$		x 60	\$
FIRST PRESENTATION OF MULTIPLE DEP. CLAIM				+ 100	\$		+200	\$
TOTAL =				\$ 0			\$	

DLEV012055

The Honorable Commissioner of  
Patents and Trademarks  
Page 2

- ☐ Please charge my Deposit Account No. 08-0380 in the amount of \$\_\_\_\_\_.
- ☐ A check in the amount of \$\_\_\_\_\_ is attached.
- ☒ A separate Petition for Extension of Time is being filed concurrently herewith.
- ☒ Payment for the extension fee is included with the petition.
- ☐ Deposit Account No. 08-0380 is being charged for the extension fee.
- ☒ The Commissioner is hereby authorized to charge payment of the following fees associated with this communication or credit any overpayment to Deposit Account No. 08-0380:
- ☒ Any filing fees under 37 C.F.R. 1.16 for the presentation of extra claims.
- ☒ Any patent application processing fees under 37 C.F.R. 1.17.

Any extensions of time that are required to maintain this application in a pending status, if not included herewith, are hereby requested. The Commissioner is hereby authorized to charge such extension fees to Deposit Account No. 08-0380. Two copies of this transmittal letter are enclosed for accounting purposes.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.



By Paula A. Campbell  
Registration No. 32,503  
Attorney for Applicant(s)  
(617) 861-6240

Dated: December 20, 1990

DLEV012056

PATENT APPLICATION

SPC89-05 Amend



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91 JAN -8 AM 10:57  
GROUP 120

7/10  
1/16/91

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Timothy J. Barberich and James W. Young

Serial No.: 07/461,262

Group Art Unit: 125

Filed: January 5, 1990 Examiner: L. Schenkman

For: METHOD FOR TREATING ASTHMA USING  
OPTICALLY PURE R(-) ALBUTEROL

AMENDMENT

The Honorable Commissioner  
of Patents and Trademarks  
Washington, D.C. 20231

Sir:

This amendment is submitted in response to the Office Action mailed from the Patent Office on August 20, 1990. A one-month extension of time for responding to the Office Action is respectfully requested. A petition for the extension of time and the appropriate fee are being submitted concurrently herewith. Please amend the above-identified application as follows:

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to Honorable Commissioner of Patents and Trademarks, Washington, D.C. 20231, on 12-20-90.  
Hamilton, Brook Smith & Reynolds

12-20-90  
Date  
Susan D. Williams  
Signature

DLEV012057

-2-

In the Claims

- Sub B2* 9. (Amended) A composition comprising a mixture of an optically pure isomer of albuterol and at least one additional drug.
- 21* 10. (Amended) A composition of Claim 9 [containing] wherein the albuterol contains at least 90% by weight of the R(-) isomer of albuterol.
11. (Amended) A composition of Claim 10 [containing] wherein the albuterol contains at least 99% by weight of the R(-) isomer of albuterol.

REMARKSApplicants' Invention

The invention is a method for treating asthma by administering to an afflicted individual an optically pure R(-) isomer of albuterol. Racemic mixtures of drugs, including albuterol, suffer from several drawbacks, including side effects associated with one isomer but not the other, and the fact that only one isomer generally has the therapeutic effect. Higher doses of the racemic mixture must be administered than of the optically pure active isomer. The present method solves many of the problems associated with racemic albuterol.

Rejection of Claims 1-12 Under 35 U.S.C. 103

Claims 1-12 are rejected under 35 U.S.C. 103 as being unpatentable over the Chemical Abstracts reference, which, the Office Action states, teaches

DLEV012058

-3-

salbutamol (albuterol) to treat asthma. The Office Action states that the determination of a particular isomer to employ would be a matter of obvious alternatives.

The Chemical Abstracts reference (89:123259) describes the results of a comparison of the bronchodilator effects in asthmatic patients of salbutamol (albuterol), a mixture of salbutamol with hydroxyzine, and a mixture of ephedrine, hydroxyzine and theophylline. The abstract reports that there was little difference between the three combinations in terms of effectiveness or side effects.

Applicants' method utilizes an optically pure isomer of albuterol to treat asthma while reducing the side effects associated with the drug, e.g., drowsiness and cardiac disturbances. Such a method is neither taught nor suggested by the cited abstract. The abstract teaches that albuterol is not any more effective in treating asthma than other known drugs, such as theophylline, and the abstract does not teach or suggest utilizing an optical isomer of albuterol or any other drug. Thus, one skilled in the art relying upon the cited reference would not have been motivated to practice the claimed method, since there is no teaching or suggestion that the active optical isomer of a drug could be administered or would be more effective than the racemic mixture if it was.

The Examiner has cited In re Adamson et al., 125 USPQ 233 (CCPA, 1960) in support of his statement that differences in activity between optical isomers is not unexpected. In this case, the claims on appeal were composition claims directed to the levo-isomer of the cited compounds. Process claims drawn to separating

DLEV012059

-4-

the levo-isomer from the dextro isomer were also considered. The CCPA upheld the Board of Appeals' decision affirming the Examiner's rejection of the claims based on prior art showing that many biological compounds exist as optical isomers and that the specific claimed compounds were known to be racemic mixtures. This case is not applicable to the instant case, in which the claims are drawn to a method of treating asthma by administering the R(-) isomer of albuterol. The art cited by the Examiner shows that racemic albuterol has been administered for treating asthma. However, there is no teaching or suggestion of administering the R(-) isomer of albuterol, or, in fact, of administering an optical isomer of any drug. This is important because optical isomers are chemically identical but may have profoundly different biological effects. For example, one isomer of a chiral compound may be biologically active while its enantiomer, which is chemically and physically identical, may have little or no biological effect, or may have adverse effects. Such behavior cannot be predicted a priori, however. Therefore, one skilled in the art would be familiar with the biological and pharmacological unpredictability of enantiomers of a compound, and the claimed method would not have been obvious to such a person relying upon the cited abstract.

Rejection of Claims 9-12 Under 35 U.S.C. 112,  
second paragraph

Claims 9-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the

DLEV012060

-5-

subject matter which Applicants regard as the invention. The Office Action states that the claims lack proportions of ingredients, and that the amount of the R isomer appears to relate to the entire composition rather than total albuterol. Claims 9-11 have been amended to more clearly recite the proportions of ingredients. The amendments to the claims obviate this rejection.

Information Disclosure Statement

An Information Disclosure Statement is being submitted herewith.

DLEV012061

-6-

CONCLUSION

In view of the amendments to the claims and the arguments presented herein, Applicants respectfully request that the above rejections be reconsidered and withdrawn.

If the Examiner believes that a telephone conversation with Applicants' attorney would be helpful in expediting prosecution of the application, the Examiner is invited to call the undersigned attorney at 617-861-6240.

Respectfully submitted,

  
Paula A. Campbell

Registration No. 32,503  
Attorney for Applicants

Lexington, MA 02173

Dated: 12/20/90

DLEV012062

DOCKET NO. SPC89-05

#90 1215

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



Applicant(s): Timothy J. Barberich and James W. Young

Serial No.: 07/461,262

Group Art Unit: 125

Filed: January 5, 1990

Examiner: L. Schenkman

METHOD FOR TREATING ASTHMA USING OPTICALLY PURE  
R(-) ALBUTEROLPETITION FOR EXTENSION OF TIMEThe Honorable Commissioner  
of Patents and Trademarks  
Washington, D. C. 20231

Sir:

The undersigned attorney petitions the Commissioner of Patents and Trademarks to extend the time for filing a Response to the Office Action dated August 20, 1990 for 1 months from November 20, 1990 to December 20, 1990.

Small EntityOther than  
Small Entity

1 month -	X \$ 50	\$ 100
2 months -	\$ 150	\$ 300
3 months -	\$ 365	\$ 730
4 months -	\$ 575	\$ 1,150

☒ Enclosed is a check in the amount of \$ 50.00 to cover the cost of the extension.

☐ Please charge Deposit Account No. 08-0380 in the amount of \$ \_\_\_\_\_ to cover the cost of the extension fee.

Any deficiency or overpayment should be charged or credited to Deposit Account No. 08-0380. A duplicate copy of this letter is enclosed.

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to Honorable Commissioner of Patents and Trademarks, Washington, D.C. 20231, on 12-20-90

Hamilton, Brook, Smith & Reynolds  
100 DL 01/07/91 07461262

Respectfully submitted,

*Paula A. Campbell*  
Paula A. Campbell

Attorney for Applicant(s)  
Registration No. 32,503  
Telephone: (617) 861-6240  
Lexington, Massachusetts 02173

Dated: December 20, 1990  
1 215 50.00 CK

*Susan Delandrea*  
Suzanne Delandrea

12-20-90  
Date

DLEV012063

SPC89-05 IDS  
PAC26  
12/11/90

PATENT APPLICATION



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1/16/91

GROUP 120  
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Timothy J. Barberich and James W. Young

Serial No: 07/461,262 Art Unit: 125

Filed: January 5, 1990 Examiner: L. Schenkman

Title: METHOD FOR TREATING ASTHMA USING  
OPTICALLY PURE R(-) ALBUTEROL

**CERTIFICATE OF MAILING**

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to Honorable Commissioner of Patents and Trademarks, Washington, D.C. 20231, on 12-30-90.

Hamilton, Brock, Smith & Reynolds

12-30-90  
Date  
Susan Dilland  
Signature

INFORMATION DISCLOSURE STATEMENT

The Honorable Commissioner  
of Patents and Trademarks  
Washington, D.C. 20231

Sir:

Pursuant to 37 C.F.R. 1.56 and 1.97-1.99, the following listed items are cited to the Examiner as being information which, in the good faith judgment of the Applicants and the undersigned Attorney may be relevant to the subject matter claimed in the above-identified application.

DLEV012064

-2-

As required by 37 C.F.R. 1.98, each item listed below is followed by a "concise explanation" of its possible relevance. The comments are merely an introduction intended to help the Examiner place each item in context. They are not represented or intended to be comprehensive summaries.

AR R.T. Brittain et al., Br. J. Pharmacol.,  
48:144-147 (1973)

Brittain and co-workers describe the pharmacological activity on  $\beta$ -adrenoreceptors of the optical isomers of salbutamol (a/k/a albuterol). They report that R(-) salbutamol was much more potent than S(+) salbutamol on  $\beta$ -adrenoreceptors.

AS C.J. Hawkins and G.T. Klease, J. Med. Chemistry,  
16(7):856-857 (1973)

Hawkins and Klease describe the potency of the (+) and (-) isomers of salbutamol (albuterol) on guinea pig tracheal tissue. They report that the (-) isomer was significantly more active than racemic salbutamol.

AT D. Hartley and D. Middlemiss, J. Med. Chemistry,  
14(9):895 (1971)

Hartley and Middlemiss describe the physical and chemical configuration of the optical isomers of salbutamol (albuterol). They report that R(-) salbutamol is much more active on  $\beta$ -adrenoreceptors than the S(+) isomer.

DLEV012065

-3-

AU C.K. Buckner and P. Abel, J. Pharmacol. Exp. Ther., 189(3):616-625 (1974)

Buckner and Abel describe the effects of the optical isomers of soteranol, trimetoquinol and salbutamol (albuterol) on the  $\beta$ -adrenergic receptors of isolated guinea pig tracheal and atrial tissue in vitro. They report that the active isomer of saltbutamol R(-) salbutamol, is much more active in tracheal tissue than in atrial tissue.

The references are listed on the attached PTO form 1449 and a copy of each is included for the Examiner's convenience.

Respectfully submitted,



Paula A. Campbell

Registration No. 32,503

Attorney for Applicants

(617) 861-6240

Lexington, MA 02173

Dated: 12/20/90

DLEV012066

Patents Act 1977

Examiner's report to the Comptroller under  
Section 17 (The Search Report)

Application Number

9207363.4

## Relevant Technical fields

(i) UK CI (Edition

K

A5B (BHA, BJA)

5

A61K

(ii) Int CI (Edition

)

Search Examiner

J F JENKINS

## Databases (see over)

(i) UK Patent Office

Date of Search

6 AUGUST 1992

ONLINE DATABASE: DIALINDEX (MEDICINE),  
(ii) CAS-ONLINE

Documents considered relevant following a search in respect of claims

1 TO 10

Category (see over)	Identity of document and relevant passages	Relevant to claim(s)
X E	WO A1 91/09596 (SEPRACOR INC) whole document	1-3, 5-9
X E	EP A1 0455155 (BOEHRINGER INGELHEIM)	1-3, 5-9
Y	Chem. Pharm. Bulet. 26(4), 1123-9, (1976) Murase et al	1-3, 5-9
Y	J. Med.Chem. 14(9), 895-6 (1971) Hartley et al	1-3, 5-9
Y	J. Liq. Chromatogr. 11, 2147-63 (1988) Okamoto et al	1-3, 5-9
Y	Biochem. Pharmacol. 35(12), 1981-5, (1986) Koster et al	1-3, 5-9
Y	Br. J. Chim. Pharmac. 27, 49-56, (1989) Borgstrom et al	1-3, 5-9

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SJJ - doc99\111,000272

DLEV012067

Category	Identity of document and relevant passages	Relevant to claim(s)
		<p style="writing-mode: vertical-rl; transform: rotate(180deg);">BEST AVAILABLE COPY</p>

**Categories of documents**

**X:** Document indicating lack of novelty or of inventive step.

**Y:** Document indicating lack of inventive step if combined with one or more other documents of the same category.

**A:** Document indicating technological background and/or state of the art.

**P:** Document published on or after the declared priority date but before the filing date of the present application.

**E:** Patent document published on or after, but with priority date earlier than, the filing date of the present application.

**&:** Member of the same patent family, corresponding document.

**Databases:** The UK Patent Office database comprises classified collections of GB, EP, WO and US patent specifications as outlined periodically in the Official Journal (Patents). The on-line databases considered for search are also listed periodically in the Official Journal (Patents).

Published 1992 at The Patent Office, Concept House, Cardiff Road, Newport, Gwent NP9 1RL. Further copies may be obtained from Sales Branch, Unit 8, Nine Mile Point, Carmichael, Cross Keys, Newport, NP1 7HZ. Printed by Multiplex Techniques Ltd, St Mary Cray, Kent.

DLEV012068


**UNITED STATES DEPARTMENT OF COMMERCE**  
**Patent and Trademark Office**

 Address: COMMISSIONER OF PATENTS AND TRADEMARKS  
 Washington, D.C. 20231

SERIAL NUMBER	FILED DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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07/461,262 01/05/90 BARBERICH

T SPC8905

EXAMINER

SCHENKMAN, L.

 HAMILTON, BROOK, SMITH & REYNOLDS  
 TWO MILITIA DRIVE  
 LEXINGTON, MA 02173-4799

ART UNIT

PAPER NUMBER

125

DATE MAILED:

03/22/91

 This is a communication from the examiner in response to your application.  
 COMMISSIONER OF PATENTS AND TRADEMARKS

☐ This application has been examined ☒ responsive to communication filed on 12-24-90 ☐ This action is made final.

 A shortened statutory period for response to this action is set to expire 3 month(s) 3 days from the date of this letter.  
 Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 135

**Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:**

- |   |  |
|---|--|
| 1. <input type="checkbox"/> Notice of References Cited by Examiner, PTO-892.        | 2. <input type="checkbox"/> Notice re Patent Drawing, PTO-848.                   |
| 3. <input checked="" type="checkbox"/> Notice of Art Cited by Applicant, PTO-1448.  | 4. <input type="checkbox"/> Notice of Informal Patent Application, Form PTO-152. |
| 5. <input type="checkbox"/> Information on How to Effect Drawing Changes, PTO-1474. | 6. <input type="checkbox"/> _____  |

**Part II SUMMARY OF ACTION**

1. ☒ Claims 1-12 are pending in the application.  
     Of the above, claims \_\_\_\_\_ are withdrawn from consideration.
2. ☐ Claims \_\_\_\_\_ have been cancelled.
3. ☐ Claims \_\_\_\_\_ are allowed.
4. ☒ Claims 1-12 are rejected.
5. ☐ Claims \_\_\_\_\_ are objected to.
6. ☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on \_\_\_\_\_. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-848).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on \_\_\_\_\_, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed \_\_\_\_\_, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received  
☐ been filed in parent application, serial no. \_\_\_\_\_; filed on \_\_\_\_\_.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other \_\_\_\_\_

EXAMINER'S ACTION

DLEV012069

Serial No. 07/461,262

-2-

Art Unit 125

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-12 are rejected under 35 U.S.C. § 103 as being unpatentable over Chemical Abstracts for reasons of record. Applicants arguments regarding unpredictability are not persuasive in view of the cited decision.

Claims 1-5 are rejected under 35 U.S.C. § 103 as being unpatentable over Brittain et al, Hartley et al, Hawkins et al and Buckner et al who teach compositions containing the claimed compounds (e.g water or saline solution) and its isomers used as a bronchodilation<sup>st</sup> in the treatment of asthma. The references further teach greater bronchodilation activity of the R (-) isomer over the S(+) isomer. The use therefor, of compositions containing mainly the R (-) isomer in the treatment of asthma is clearly rendered obvious by the prior art.

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Art Unit 125

Claims 6-12 are rejected under 35 U.S.C. § 103 as being unpatentable over the references supra in further view of Chemical Abstracts which shows combination of drugs, including salbutomal, used in the treatment of asthma.

Claims 6 and 9-11 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. No basis for the mixture of isomers set forth in claims 10 and 11 can be found in claim 9 which is limited to a single isomer. Claim 9 is incorrect is not including the R(-) isomer. Compare with original claim 9. Claims 9-12 are again deemed to be too broad absent proportions of ingredients. The term "additional drug" (claims 6 and 9-11) is too broad.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. Schenkman whose telephone number is (703) 308-0091.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.



LEONARD SCHENKMAN  
EXAMINER  
ART UNIT 125

SCHENKMAN:drb  
March 13, 1991

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U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICE

ATTY. DOCKET NO.  
SPC89-05

APPLICANT  
Timothy J. Barberich, et al.

FILING DATE  
January 5, 1990

GROUP  
125

LIST OF ART CITED BY APPLICANT  
(Use several sheets if necessary)

MAIL ROOM  
DEC 24 1990  
TRADE MARK

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	AB					
	AC					
	AD					
	AE					
	AF					
	AG					
	AH					
	AI					
	AJ					
	AK					

FOREIGN PATENT DOCUMENTS

DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION
					YES
AL					
AM					
AN					
AO					
AP					

OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

AR	R.T. Brittain et al., <u>Br. J. Pharmacol.</u> , 48:144-147 (1973)
AS	C.J. Hawkins and G.T. Klease, <u>J. Med. Chemistry</u> , 16(7):856-857 (1973)
AT	D. Hartley and D. Middlemiss, <u>J. Med. Chemistry</u> , 14(9):895 (1971)

EXAMINER  
L. Barberich

DATE CONSIDERED

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Sheet 2 of 2

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CKET NO. SPC89-05

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Timothy J. Barberich and James W. Young

Serial No.: 07/461,262

Group Art Unit: 125

Filed: January 5, 1990

Examiner: L. Schenkman

For:

METHOD FOR TREATING ASTHMA USING OPTICALLY  
PURE R(-) ALBUTEROL

## CERTIFICATE OF MAILING

I hereby certify that this correspondence is being  
deposited with the United States Postal Service as First  
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Commissioner of Patents and Trademarks, Washington,  
D.C. 20231, on 9/27/91.  
Hamilton, Brook, Smith & Reynolds

The Honorable Commissioner of  
Patents and Trademarks  
Washington, D.C. 20231

Sir:

B. J. Kennedy  
Signature

9/27/91  
Date

Transmitted herewith is a response in the above-identified  
application.

☒ Small entity status of this application under 37 C.F.R. 1.9  
and 1.27 has been established by a verified statement  
previously submitted.

☐ A verified statement to establish small entity status under  
37 C.F.R. 1.9 and 1.27 is enclosed.

The fee has been calculated as shown below:

(Col. 1)		(Col. 2)		(Col. 3)	SMALL ENTITY		OTHER THAN SMALL ENTITY			
	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NO. PREVIOUSLY PAID FOR	PRESENT EXTRA		RATE	ADDIT. FEE	- OR	RATE	ADDIT. FEE
TOTAL	* 10	MINUS	** .20	= 0	x 10	\$ 0			x 20	\$
S.	* 3	MINUS	*** .3	= 0	x 30	\$ 0			x 60	\$
FIRST PRESENTATION OF MULTIPLE DEP. CLAIM					+ 100	\$			+200	\$
TOTAL =						\$ 0				\$

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